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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,692	07/28/2003	Brent L. Atkinson	CRM-P15F/P	5172

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EXAMINER	
BRADLEY, CHRISTINA	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
07/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/628,692	ATKINSON ET AL.	
	Examiner	Art Unit	
	Christina Marchetti Bradley	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/17/2008 has been entered.

2. Claims 1-14 and 19 are pending. All previous grounds of rejection are withdrawn. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 4, 5, 8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Gertzman *et al.* (U.S. Patent No. 6,030,645). Claim 1 is drawn to a bone repair putty material comprising at least about 50 weight percent of a porous, resorbable particulate derived of anorganic bone mineral or natural bone-derived material or hydroxylapatite, and a resorbable carrier gel. The instant specification does not explicitly define the term "about". Gertzman *et al.* teach a bone repair putty material comprising 30 or 33% bone particulate, cortical allograft bone powder, and a carrier component either 2 or 3% hyaluronic acid, 20 % dextran 40 PM, 20% Pluronic acid F127 or 20% Pluronic acid F108 (Table 1, examples I and IV-VIII). Gertzman *et*

al. teach that these compositions are putty with excellent formability (Table 1). With respect to claim 1, the porous, resorbable particulate is cortical allograft bone powder, 30 or 33% is at least about 50 weight percent, and the resorbable carrier gel is hyaluronic acid, dextran 40 PM, Pluronic acid F127 or Pluronic acid F108. In addition, Gertzman *et al.* teach a bone repair putty material comprising 50% cortical allograft bone powder and a carrier either 20% pluronic F127, 20% pluronic F108 or 3% chitosan (Table 1, examples II, III, XII or XIII). Gertzman *et al.* teach that these compositions are putty with poor formability. Putties with poor formability are not excluded from the scope of claim 1. With respect to claims 4 and 5, the carrier is a polysaccharide, hyaluronic acid (example I). With respect to claim 8, 2% is about 25-70%. With respect to claim 10, 30% bone powder is about 55% particulate and 2% hyaluronic acid is about 45% hyaluronic acid. Gertzman *et al.* do not explicitly teach that the putty can facilitate bone repair while migration and expansion of the particulate is minimized. Because the chemical composition of the material taught by Gertzman *et al.* is identical to the claimed composition, the prior art reference of Gertzman *et al.* inherently meets this functional limitation.

5. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Ewers *et al.* (U.S. Patent No. 6,428,803). Ewers *et al.* teach a moldable hydroxylapatite composition comprising a calcium-containing granular filler and a hydroxylapatite carrier gel, wherein the hydroxylapatite gel and the granular filler are present in a ratio of from 1:5 to 1:8 by weight (claims 1 and 12). Ewers *et al.* teach a moldable composition comprising hydroxylapatite gel mixed in a ratio of 1:10 by weight with a granular hydroxylapatite material produced from calcareous red algae (example 2). The granular filler is present at greater than 50 weight percent in the compositions taught by Ewers *et al.* Ewers *et al.* do not explicitly teach that the composition is a putty or that

it can facilitate bone repair while migration and expansion of the particulate is minimized. Because the chemical composition of the material taught by Ewers *et al.* is identical to the claimed composition, the prior art reference of Ewers *et al.* inherently meets this functional limitation.

6. Claims 1, 4 and 12 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Peterson *et al.* (US 2002/0071827). Peterson *et al.* teach a putty bone graft substitute composition having the following formulation: 100 parts by weight of medical grade calcium sulfate hemihydrate (MGCSH), 11.1 parts by weight of carboxymethylcellulose (CMC), and 47 parts by weight of sterile water (preferred embodiment 2). The putty bone graft substitute composition has the following characteristic/criteria: Handability - the resultant composition should: (a) be a single cohesive bolus; (b) be able to be handled and manipulated with minimal to no material transfer (sticking) to latex gloved hand; (c) be able to be handled without material crumbling or falling apart; and (d) exhibit minimal cracking or "tearing" with extreme manipulation, e.g., hard squeezing; and Robustness - the resultant composition, after being placed or injected into or onto the desired location, should be able to withstand body fluids, reasonable irrigation fluids and/or suctioning with minimal material erosion, disintegration or dissolution. With respect to claim 1, the porous particulate is MGCSH, which is derived from anorganic bone mineral, the MGCSH is at a concentration greater than 50 weight percent, and the carrier is carboxymethylcellulose. With respect to claims 4 and 12, the carrier is a polysaccharide, carboxymethylcellulose.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 4-6 and 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gertzman *et al.* (U.S. Patent No. 6,030,645). Claim 1 is drawn to a bone repair putty material comprising at least about 50 weight percent of a porous, resorbable particulate derived of anorganic bone mineral or natural bone-derived material or hydroxylapatite, and a resorbable carrier gel. Gertzman *et al.* teach a bone repair putty material comprising 30 or 33% bone particulate, cortical allograft bone powder, and a carrier component either 2 or 3% hyaluronic acid, 20 % dextran 40 PM, 20% Pluronic acid F127 or 20% Pluronic acid F108 (Table 1, examples I and IV-VIII). Gertzman *et al.* teach that these compositions are putty with excellent formability. In addition, Gertzman *et al.* teach a bone repair putty material comprising 50% cortical allograft bone powder and a carrier either 20% pluronic F127, 20% pluronic F108 or 3% chitosan (Table 1, examples II, III, XII or XIII). Gertzman *et al.* teach that these compositions are putty with poor formability. With respect to claims 4 and 5, the carrier is a polysaccharide, hyaluronic acid (example I). With respect to claim 8, 2% is about 25-70%. With respect to

claim 10, 30% bone powder is about 55% particulate and 2% hyaluronic acid is about 45% hyaluronic acid.

Gertzman *et al.* do not teach bone repair putty materials comprising 50% bone particulate and 40-64% carrier gel.

It would have been obvious to adjust the composition taught by Gertzman *et al.* to optimize the level of formability. The skilled artisan would have been motivated to do so based on the teaching of Gertzman *et al.* that malleable putty may be used to correct surgical defects and that it is "important to have the defect filler in the form of a stable, viscous putty to facilitate the placement of the bone growth medium into the surgical site which is usually uneven in shape and depth" (col. 1, lns. 13-24). The skilled artisan would have been particularly motivated to optimize the formability of the composition containing the highest concentration of bone particulate based on the teaching of Gertzman *et al.* that it is desirable to maximize "the amount of bone in the formulation without creating a gritty, less malleable characteristic" (col. 4, lns. 30-35). The skilled artisan would have optimized the formability by adjusting the variables recited in Table 1, namely the concentration of carrier and the particle size of the bone particulate. The skilled artisan would have focused on the compositions containing the highest concentration of bone particulate, 50% (examples II, III, XII or XIII). Gertzman *et al.* state that the putty with 50% bone particulate and poor formability is "too grainy, too dry" (Table 1). It would have been obvious to reduce graininess and dryness of these compositions by increasing the carrier concentration. It would have been further obvious to increase the bone concentration in putty compositions with excellent formability (examples I and IV-VIII) and to adjust the carrier concentration accordingly to maximize bone concentration and maintain formability. There

would have been a reasonable expectation of success given that varying concentration of active ingredients in a composition is routine experimentation. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

9. Applicant traversed the previous rejection based on Gertzman *et al.* on the grounds that:

> ... a person of ordinary skill in the art looking at the teachings in Gertzman and applying common sense, would not reasonably consider adding bone particulate at concentrations of 50 wt.% and greater. There is absolutely no basis in the teachings of Gertzman for making such putty material. At bone powder concentrations of 50%, the Gertzman putty materials show poor formability and are simply unacceptable. Gertzman repeatedly provides evidence of these problems. (See Examples II [50% particulate conc.], III [50%], XII [50%], and XIII [50%].)

This argument is not persuasive. It is true that a person of ordinary skill in the art would not use the compositions having poor formability in bone repair applications. However, given the stated goal of Gertzman *et al.* to maximize the amount of bone particulate in the putty while maintaining formability, and the importance of formability in applications of the compositions, the skilled artisan would have been motivated to improve the compositions with the highest concentration of bone particulate, those containing 50 weight percent.

Applicant further traversed the previous rejection based on Gertzman *et al.* on the grounds that:

> Gertzman provides no guidance or suggestion as to how to make bone repair putty having good handling and molding properties at > 50% concentrations. Merely trying different ingredients and optimizing their amounts is not enough. Many different factors were considered in making Applicants' materials. Gertzman does not provide the skilled artisan with any reasonable expectation that such materials would even work. Thus, a skilled artisan looking at Gertzman would only be motivated or guided to make the presently claimed putty material by looking at Applicants' own specification. It is respectfully submitted that such hindsight reconstruction of the claimed invention to render it prima facie obvious is not permitted.

This argument is not persuasive. The skilled artisan would use common sense to reason that in order to reduce dryness and graininess, one could increase the amount of carrier in the

composition. Such reasoning would not require hindsight reconstruction of the claimed invention and could be arrived at based solely on the teaching of Gertzman *et al.* that carriers are important for creating the malleable and formable properties of bone particulate-containing putty.

10. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gertzman *et al.* (U.S. Patent No. 6,030,635) as applied to claims 1, 4-6 and 8-11 above, in further view of Tofe (US 2003/0143283). With respect to claim 2, Gertzman *et al.* teach that the particle size of the cortical allograft bone powder is 250-420, 420-850 or 100-300 microns (examples I and IV-VIII). Gertzman *et al.* do not teach that the bone particulate material is derived from bovine. Tofe teaches that bovine bone ground or milled to a suitable small-sized grain or to a powder (paragraph 0012) may be combined with a carrier such hyaluronate for use in a bone repair material (paragraph 0013). It would have been obvious to use bovine bone particles in the compositions taught by Gertzman *et al.* The skilled artisan would have been motivated to do so and there would have been a reasonable expectation of success given the teaching of Peterson *et al.* that the bovine-derived bone particles can be combined with hyaluronate for use in a bone repair composition. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

11. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gertzman *et al.* (U.S. Patent No. 6,030,635) as applied to claims 1, 4-6 and 8-11 above, in further view of Ewers *et al.* (U.S. Patent No. 4,770,860). Gertzman *et al.* do not teach that the bone particulate material is derived from algae. Ewers *et al.* teach a porous hydroxyl apatite material made from calcium-rich basic skeletons of lime-encrusting algae converted into hydroxyl apatite (abstract). It would

have been obvious to one of ordinary skill in the art to substitute the hydroxylapatite material of Ewers *et al.* for the bone particulate in the compositions taught by Gertzman *et al.* The skilled artisan would have been motivated to do so and there would have been a reasonable expectation of success given the teaching of Ewers *et al.* that the hydroxylapatite material can be used for artificial bone, artificial tooth root, augmentation material, stabilization material, artificial hollow bodies or defect filling material. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

12. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gertzman *et al.* (U.S. Patent No. 6,030,635) as applied to claims 1, 4-6 and 8-11 above, in further view of Peterson *et al.* (US 2002/0071827). Gertzman *et al.* do not teach that the carrier is hydroxypropyl cellulose or methyl cellulose. Peterson *et al.* teach a putty bone graft substitute composition having the following formulation: 100 parts by weight of medical grade calcium sulfate hemihydrate (MGCSH), 11.1 parts by weight of carboxymethylcellulose (CMC), and 47 parts by weight of sterile water (preferred embodiment 2). The putty bone graft substitute composition has the following characteristic/criteria: Handability - the resultant composition should: (a) be a single cohesive bolus; (b) be able to be handled and manipulated with minimal to no material transfer (sticking) to latex gloved hand; (c) be able to be handled without material crumbling or falling apart; and (d) exhibit minimal cracking or "tearing" with extreme manipulation, e.g., hard squeezing; and Robustness - the resultant composition, after being placed or injected into or onto the desired location, should be able to withstand body fluids, reasonable irrigation fluids and/or suctioning with minimal material erosion, disintegration or dissolution. It would have been obvious to one of ordinary skill in the art to use the

carboxymethylcellulose of Peterson *et al.* as a carrier in the compositions taught by Gertzman *et al.* The skilled artisan would have been motivated to do so and there would have been a reasonable expectation of success given the teaching of Peterson *et al.* that hyaluronic acid or a cellulose derivative such as methylcellulose, carboxymethylcellulose, methylcellulose, hydroxypropyl cellulose, hydroxypropyl methyl cellulose, ethylcellulose, hydroxyethylcellulose, and/or cellulose acetate butyrate may be used in the putty bone graft substitute (preferred embodiment 5). Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

13. Claims 7, 13, 14 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gertzman *et al.* (U.S. Patent No. 6,030,635) as applied to claims 1, 4-6 and 8-11 above, in further view of Bhatnager (U.S. Patent No. 5,635,482). Gertzman *et al.* do not teach that the bone repair composition further comprises at least one P-15 synthetic biomimetic polypeptide sequence of Type I collagen bound to the bone particulate. Bhatnager teaches a family of synthetic peptides are provided that mimic the cell binding domain or P-15 domain of collagen (col. 3, lns. 29-48 and col. 4, ln.16). Bhatnager teaches that these P-15 mimetics can be used to coat particulate hydroxylapatite (example 4) for incorporation into a carrier gel and use in orthopedic applications such as bone filling/fusion for osteoporosis and other bone diseases, cartilage repair for arthritis and other joint diseases, and tendon repair (col. 10, lns. 50-56). It would have been obvious to use the P-15 mimetic peptides taught by Bhatnager to coat the bone particles in the bone repair composition taught by Gertzman *et al.* The skilled artisan would have been motivated to do so based on the teaching by Bhatnager that the peptides facilitate cell binding and that when the coated particles were in a gel that also included inventive peptide,

there was a very large influx of cells into the gel that organized on and around the coated particles in tissue-like masses (example 4). There would have been a reasonable expectation of success given Bhatnager demonstrate that the peptides can be used to coat synthetic bone particles. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Marchetti Bradley whose telephone number is (571)272-9044. The examiner can normally be reached on Monday-Thursday, 9:00 A.M. to 3:00 P.M.

16. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

17. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654

/Christina Marchetti Bradley/
Examiner, Art Unit 1654

cmb